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      S3      47  RD (unique items)
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S1	2511	INTRON? (S) (STABLE OR STABILI?) (S) (INCREAS? OR ENHANC?)
S2	55	S1 AND RECOMBINANT? AND NUCLEIC
S3	47	RD (unique items)

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      S3      47  RD (unique items)
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S3	47	RD (unique items)

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Set	Items	Description
S1	2511	INTRON? (S) (STABLE OR STABILI?) (S) (INCREAS? OR ENHANC?)
S2	55	S1 AND RECOMBINANT? AND NUCLEIC
S3	47	RD (unique items)

>>>KWIC option is not available in file(s): 399

3/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011894725 BIOSIS NO.: 199900154385
Fibroblast growth factor-8 expression is regulated by intronic engrailed and Pbx1-binding sites
AUTHOR: Gemel Joanna; Jacobsen Christina; Macarthur Craig A (Reprint)
AUTHOR ADDRESS: Washington Univ. Sch. Med., Dep. Pediatr., Campus Box 8116, One Children's Place, St. Louis, MO 63110, USA**USA
JOURNAL: Journal of Biological Chemistry 274 (9): p6020-6026 Feb. 26, 1999 1999
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: the vertebrate embryo. We now report on the identification of regions of Fgf8 important for its transcriptional regulation in murine ES cell-derived embryoid bodies. *Stable* transfection of ES cells, using a human growth hormone reporter gene, was employed to identify regions of the Fgf8 gene with promoter/*enhancer* activity. A 2-kilobase 5' region of Fgf8 was shown to contain promoter activity. A 0.8-kilobase fragment derived from the large *intron* of Fgf8 was found to *enhance* human growth hormone expressed from the Fgf8 promoter 3-4-fold in an orientation dependent manner. The *intronic* fragment contains DNA-binding sites for the AP2, Pbx1, and Engrailed transcription factors. Gel shift and Western blot experiments documented the presence of these transcription...

...nuclear extracts from ES cell embryoid bodies. In vitro mutagenesis of the Engrailed or Pbx1 site demonstrated that these sites modulate the activity of the *intronic* fragment. In addition, in vitro mutagenesis of both Engrailed and Pbx1 sites indicated that other unidentified sites are responsible for the transcriptional *enhancement* observed with the *intronic* fragment.
DESCRIPTORS:
...METHODS & EQUIPMENT: analytical method, *nucleic* acid labeling...

...*Recombinant* DNA Technology, genetic engineering method...

...*Recombinant* DNA Technology, sequencing techniques, sequencing method

3/3,K/2 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

02403637 2003186510
Novel functional role of CA repeats and hnRNP L in RNA stability
Hui J.; Reither G.; Bindereif A.
ADDRESS: A. Bindereif, Institut fur Biochemie, Justus-Liebig-Universitat Giessen, Heinrich-Buff-Ring 58, D-35392 Giessen, Germany
EMAIL: albrecht.bindereif@chemie.bio.uni-giessen.de
Journal: RNA, 9/8 (931-936), 2003, United States
PUBLICATION DATE: August 1, 2003
CODEN: RNARF
ISSN: 1355-8382
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 15

CA dinucleotide repeat sequences are very common in the human genome. We have recently demonstrated that the polymorphic CA repeats in *intron* 13 of the human endothelial nitric oxide synthase (eNOS) gene function as an unusual, length-dependent splicing *enhancer*. The CA repeat *enhancer* requires for its activity specific binding of hnRNP L. Here we show that in the absence of bound hnRNP L, the pre-mRNA is cleaved directly upstream of the CA repeats. The addition of *recombinant* hnRNP L restores RNA *stability*. CA repeats are both necessary and sufficient for this specific cleavage in the 5prime adjacent RNA sequence. We conclude that - in addition to its role...

CLASSIFICATION CODE AND DESCRIPTION:
...*Nucleic* Acid Structure and Biophysics

3/3,K/3 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

04004118 H.W. WILSON RECORD NUMBER: BGSI99004118 (USE FORMAT 7 FOR FULLTEXT)
Alternative splicing of pre-mRNA: developmental consequences and mechanisms of regulation.
Lopez, A. Javier
Annual Review of Genetics (Annu Rev Genet) v. 32 ('98) p. 279-305
SPECIAL FEATURES: bibl il ISSN: 0066-4197
LANGUAGE: English

COUNTRY OF PUBLICATION: United States
WORD COUNT: 13032

(USE FORMAT 7 FOR FULLTEXT)

TEXT:
... stabilize binding of U2AF to the RNA or form a bridge to U1 snRNP at the 5' splice site (72, 143, 149; but see 103).

ENHANCEMENT OF SPLICE SITE RECOGNITION
Recognition of a particular splice ...site can be ensured by a strong match to the consensus sequence or by the assistance of cis-acting elements and transacting factors. Across short *introns*, U1 snRNP at the 5' splice site and U2AF at the polypyrimidine tract can interact through extrinsic factors to *stabilize* binding and juxtapose the splice sites in a commitment complex (reviewed in 14, 99). When internal exons are flanked by longer *introns*, interactions can occur across the exon to *stabilize* the binding of U2AF and U1 snRNP (reviewed in 9, 14). These exon bridging interactions are limited to exons between 50 and 500 nt long...

...is too large for effective interaction. When the distances between splice sites are not propitious, or when a splice site is inherently weak, cis-acting *enhancers* can help recruit the essential splicing factors (14, 22). Splicing *enhancers* can be position-dependent; most are located close to the splice site that they activate, and changing their location can alter their dependence on particular...binds to a poly(U) run in the polypyrimidine tract of the regulated 3' splice site (67, 111, 121, 135), and in vitro experiments with *recombinant* proteins show that binding of SXL precludes binding by U2AF (135). If the RS domain of U2AF65 is attached to SXL, however, SXL is transformed...

...cases has also been attributed to reduced access of U2AF to the polypyrimidine tract because binding competition can be demonstrated in vitro and preincubation with *recombinant* U2AF counteracts the PTB-dependent inhibition (26, 76, 121). However, it is not clear whether PTB functions in vivo as an alternative splicing factor or...required for effective repression of IVS3 splicing (56).

What, if any, is the role of U1 snRNP in the repressor complex? It may help to *stabilize* the complex, whose principal function may be to block access to the authentic 5' splice site. U1 snRNP may itself hinder access to this splice...

...to serve a regulatory role. Recruitment of U1 snRNP to regulatory elements also occurs in other systems. U1 snRNP associates with some vertebrate exonic splicing *enhancers* (123, 142) and with a 5' splice site consensus sequence within an *intronic* element that stimulates a regulated cleavage/polyadenylation site in the pre-mRNA for calcitonin/calcitonin gene-related peptide (CT/CGRP) (81). Although the functional significance is not known in the former cases, *enhancement* of in vitro poly-adenylation in the CT/CGRP RNA requires U1 RNA. The involvement of PSI in recruiting U1 snRNP to the F1 pseudo...

...splicing factors, on the other. Substantial experimental and correlational evidence has implicated SR proteins as dose-dependent positive regulators that influence alternative splicing decisions through *stabilization* of U1 snRNP binding or *enhancer* activation (reviewed in 23, 44, 86, 139). Another example may be the KH domain protein KSRP. Inclusion of the c-src N1 exon requires the cooperative assembly of an

intronic activator complex that depends critically on KSRP; KSRP is enriched in neuronal cells, where N1 is normally included, but it is not restricted to this...DS, Fresco LD, Keene JD. 1992. RNA specificity of a Drosophila snRNP protein that shares sequence homology with mammalian U1-A and U2-B proteins. *Nucleic* Acids Res. 20:3645-50

59. Hedley ML, Maniatis T. 1991. Sex-specific splicing and polyadenylation of dsx pre-mRNA requires a sequence that binds...Sakamoto H, Inoue K, Higuchi I, Ono Y, Shimura Y. 1992. Control of Drosophila Sex-lethal pre-mRNA splicing by its own female-specific product. *Nucleic* Acids Res. 20:5533-40

109. Salz HK. 1992. The genetic analysis of snf: a Drosophila sex determination gene required for activation of Sex-lethal...

3/3,K/4 (Item 1 from file: 155)

18028150 PMID: 15632113

Triticum durum metallothionein. Isolation of the gene and structural characterization of the protein using solution scattering and molecular modeling.

Bilecen Kivanc; Ozturk Umit H; Duru Adil D; Sutlu Tolga; Petoukhov Maxim V; Svergun Dimitri I; Koch Michel H J; Sezerman Ugur O; Cakmak Ismail; Sayers Zehra

Sabanci University, Faculty of Engineering and Natural Sciences, 34956, Orhanli, Tuzla, Istanbul, Turkey.

Journal of biological chemistry (United States) Apr 8 2005, 280 (14) p13701-11, ISSN 0021-9258 Journal Code: 2985121R

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

A novel gene sequence, with two exons and one *intron*, encoding a metallothionein (MT) has been identified in durum wheat Triticum durum cv. Balcali85 genomic DNA. Multiple alignment analyses on the cDNA and the translated...

... residue-long hinge region devoid of cysteines. dMT was overexpressed in Escherichia coli as a fusion protein (GSTdMT), and bacteria expressing the fusion protein showed *increased* tolerance to cadmium in the growth medium compared with controls. Purified GSTdMT was characterized by SDS- and native-PAGE, size exclusion chromatography, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry. It was shown that the *recombinant* protein binds 4 +/- 1 mol of cadmium/mol of protein and has a high tendency to form *stable* oligomeric structures. The structure of GSTdMT and dMT was investigated by synchrotron x-ray solution scattering and computational methods. X-ray scattering measurements indicated a strong tendency for GSTdMT to form dimers and trimers in solution and yielded structural models that were compatible with a *stable* dimeric form in which dMT had an extended conformation. Results of homology modeling and ab initio solution scattering approaches produced an elongated dMT structure with...

...; chemistry--CH; Metallothionein--genetics--GE; Metallothionein --metabolism--ME; Models, Molecular; Molecular Sequence Data; Plant Proteins--chemistry--CH; Plant Proteins--genetics--GE; Plant Proteins --metabolism--ME; *Recombinant* Fusion Proteins--chemistry--CH; *Recombinant* Fusion Proteins--genetics--GE; *Recombinant* Fusion Proteins

--metabolism--ME; Sequence Alignment; Sequence Homology, *Nucleic* Acid
Chemical Name: Plant Proteins; *Recombinant* Fusion Proteins; Cadmium; Metallothionein

3/3,K/5 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15018324 PMID: 14561886
The roles of endonucleolytic cleavage and exonucleolytic digestion in the 5'-end processing of S. cerevisiae box C/D snoRNAs.
Lee Chrissie Young; Lee Albert; Chanfreau Guillaume
Department of Chemistry and Biochemistry and the Molecular Biology Institute, University of California Los Angeles, Los Angeles, California 90095-1569, USA.
RNA (New York, N.Y.) (United States) Nov 2003, 9 (11) p1362-70, ISSN 1355-8382 Journal Code: 9509184
Contract/Grant No.: GM07185; GM; NIGMS; GM0896; GM; NIGMS; R01-GM61518; GM; NIGMS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Small nucleolar RNAs (snoRNAs) play important roles in ribosomal RNA metabolism. In Saccharomyces cerevisiae, box C/D snoRNAs are synthesized from excised *introns* , polycistronic precursors, or independent transcription units. Previous studies have shown that only a few independently transcribed box C/D snoRNAs are processed at their 5...

... were identified in vivo when the 5' --> 3' exonucleases Xrn1p and Rat1p are inactivated (xrn1delta rat1-1) and in vitro using model RNA substrates and *recombinant* Rnt1p. Some of these snoRNAs show *increased* levels of unprocessed precursors when the rnt1Delta deletion is combined to the xrn1delta rat1-1 mutation, suggesting that these exonucleases participate in the 5' processing...

...Unprocessed precursors are not significantly destabilized in the absence of the trimethylguanosine capping enzyme Tgs1p, suggesting that a 5' monomethyl cap is sufficient to ensure *stabilization* of these precursors. These results demonstrate that the majority of independently transcribed box C/D snoRNAs from the yeast genome undergo 5'-end processing and...
; Base Sequence; Hydrolysis; Molecular Sequence Data; *Nucleic* Acid Conformation; RNA, Fungal--chemistry--CH; RNA, Small Nucleolar--chemistry --CH; *Recombinant* Proteins--metabolism--ME
Chemical Name: RNA, Fungal; RNA, Small Nucleolar; *Recombinant* Proteins; Endonucleases; Exonucleases

3/3,K/6 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13944811 PMID: 11698502
A highly conserved c-fms gene intronic element controls macrophage-specific and regulated expression.
Himes S R; Tagoh H; Goonetilleke N; Sasmono T; Oceandy D; Clark R;

Bonifer C; Hume D A
Institute for Molecular Bioscience, University of Queensland, Brisbane 4072, Australia.
Journal of leukocyte biology (United States) Nov 2001, 70 (5) p812-20, ISSN 0741-5400 Journal Code: 8405628
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... encodes the receptor for macrophage colony-stimulating factor-1. This gene is expressed selectively in the macrophage cell lineage. Previous studies have implicated sequences in *intron* 2 that control transcript elongation in tissue-specific and regulated expression of c-fms. Four macrophage-specific deoxyribonuclease I (DNase I)-hypersensitive sites (DHSs) were identified within mouse *intron* 2. Sequences of these DHSs were found to be highly conserved compared with those in the human gene. A 250-bp region we refer to as the fms *intronic* regulatory element (FIRE), which is even more highly conserved than the c-fms proximal promoter, contains many consensus binding sites for macrophage-expressed transcription factors including Sp1, PU.1, and C/EBP. FIRE was found to act as a macrophage-specific *enhancer* and as a promoter with an antisense orientation preference in transient transfections. In *stable* transfections of the macrophage line RAW264, as well as in clones selected for high- and low-level c-fms mRNA expression, the presence of *intron* 2 *increased* the frequency and level of expression of reporter genes compared with those attained using the promoter alone. Removal of FIRE abolished reporter gene expression, revealing a suppressive activity in the remaining *intronic* sequences. Hence, FIRE is shown to be a key regulatory element in the fms gene.
...; Genes, Reporter; Humans; Luciferases--biosynthesis--BI; Luciferases --genetics--GE; Mice; Molecular Sequence Data; Oligodeoxyribonucleotides, Antisense--genetics--GE; Oligonucleotide Array Sequence Analysis; RNA, Messenger--biosynthesis--BI; *Recombinant* Fusion Proteins--biosynthesis --BI; Regulatory Sequences, *Nucleic* Acid; Sequence Alignment; Sequence Homology, *Nucleic* Acid; Transcription Factors--metabolism--ME; Transfection
Chemical Name: Oligodeoxyribonucleotides, Antisense; RNA, Messenger; *Recombinant* Fusion Proteins; Transcription Factors; Luciferases; Receptor, Macrophage Colony-Stimulating Factor; Deoxyribonuclease I

3/3,K/7 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12610594 PMID: 10410675
A role for RNA processing in regulating expression from transfected genes.
McBurney M W; Yang X; Jardine K; Cormier M
Ottawa Regional Cancer Center, University of Ottawa, Canada. michael mcburney@cancercare.on.ca
Somatic cell and molecular genetics (UNITED STATES) Jul 1998, 24 (4) p203-15, ISSN 0740-7750 Journal Code: 8403568
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM

Record type: MEDLINE; Completed

We have examined the expression of cloned genes following their *stable* integration into the genome of pluripotent embryonal carcinoma stem cells. Transfected genes integrate into the genome as tandem arrays. Expression of reporter genes from these...

... in embryonal carcinoma cells is inefficient probably because genes are subject to repeat-induced gene silencing. We found that expression of reporter genes was significantly *enhanced* if co-transfected with cloned fragments derived from the murine Pgk-1 gene. The *enhanced* expression required (a) that the Pgk-1 fragment carries an active promoter, (b) that the promoter drives transcription through a region of more than 12 kbp, and (c) that this transcribed region contains both *introns* and exons. Reporter gene activity did not require specific Pgk-1 DNA sequences suggesting that the coupled processes of transcription and RNA processing conferred activity...

...; and inhibitors--AI; Histone Deacetylases--metabolism--ME; Introns --genetics--GE; Lac Operon--genetics--GE; Mice; Phosphoglycerate Kinase --metabolism--ME; Plasmids--genetics--GE; Promoter Regions (Genetics); *Recombinant* Fusion Proteins--drug effects--DE; *Recombinant* Fusion Proteins--genetics--GE; *Recombinant* Fusion Proteins--metabolism--ME; Recombination, Genetic; Repetitive Sequences, *Nucleic* Acid; Transcription, Genetic; Transfection; Tumor Cells, Cultured; beta-Galactosidase--drug effects--DE; beta-Galactosidase--genetics--GE; beta-Galactosidase--metabolism--ME

Chemical Name: Butyrates; Plasmids; *Recombinant* Fusion Proteins; Phosphoglycerate Kinase; beta-Galactosidase; Histone Deacetylases

3/3,K/8 (Item 5 from file: 155)

11634153 PMID: 8945637

Human kinesin light (beta) chain gene: DNA sequence and functional characterization of its promoter and first exon.

Chernajovsky Y; Brown A; Clark J

Kennedy Institute of Rheumatology, Molecular Biology Laboratory, Hammersmith, London, UK.

DNA and cell biology (UNITED STATES) Nov 1996, 15 (11) p965-74, ISSN 1044-5498 Journal Code: 9004522

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... system, producing a 70-kDa protein. Using this cDNA as a probe, we isolated and sequenced the promoter, first exon, and part of the first *intron* of this gene from a genomic lambda EMBL3 human placental DNA library. The whole gene spans more than 90 kb. The beta kinesin promoter region...

... of beta kinesin was 75-fold more active than the HSV-tk promoter. The first exon contains the 5'-untranslated sequence capable of forming a *stable* double-hairpin loop, which functions as a translational *enhancer* . Its deletion decreases the efficiency of in vitro translation of beta kinesin mRNA and confers *increased* translation to a CAT reporter gene.

...; Cell Line; Cell-Free System; Chloramphenicol O-Acetyltransferase --biosynthesis--BI; Dogs; Gene Library; Hela Cells; Humans; Macromolecular Substances; Microsomes--metabolism--ME; Molecular Sequence Data; Neuroblastoma; *Nucleic* Acid Conformation; Open Reading Frames; Pancreas --metabolism--ME; Placenta--metabolism--ME; Pregnancy; Protein Biosynthesis ; Protein Processing, Post-Translational; RNA, Messenger--chemistry--CH; RNA, Messenger--metabolism--ME; *Recombinant* Fusion Proteins --biosynthesis--BI; Transcription, Genetic; Transfection

Chemical Name: Macromolecular Substances; RNA, Messenger; *Recombinant* Fusion Proteins; Chloramphenicol O-Acetyltransferase; Kinesin

3/3,K/9 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10999590 PMID: 7540041

Efficient protein-facilitated splicing of the yeast mitochondrial bI5 intron.

Weeks K M; Cech T R

Department of Chemistry and Biochemistry, Howard Hughes Medical Institute, University of Colorado, Boulder 80309-0215, USA.

Biochemistry (UNITED STATES) Jun 13 1995, 34 (23) p7728-38, ISSN 0006-2960 Journal Code: 0370623

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The splicing factor CBP2 is required to excise the yeast mitochondrial group I *intron* bI5 in vivo and at low magnesium ion concentrations in vitro. CBP2 binding is strengthened 20-fold by *increasing* Mg2+ concentrations from 5 to 40 mM, implying the protein binds, in part, to the same structure as that *stabilized* by the cation. The same transition is also observed as a cooperative *increase* in the rate of self-processing between 5 and 40 mM Mg2+, providing strong evidence for an RNA folding transition promoted by either Mg2+ or...

... evidence that kcat is limited by chemistry at low pH and by a conformational step at high pH. Because binding by either Mg2+ or CBP2 *increases* the rate of chemistry more than the rate of the conformational step, in the physiological pH range (7-7.6) the protein-facilitated reaction is...

; Base Sequence; Hydrogen Bonding; Introns; Kinetics; Magnesium --metabolism--ME; Molecular Sequence Data; *Nucleic* Acid Conformation; RNA-Binding Proteins--chemistry--CH; *Recombinant* Proteins; Saccharomyces cerevisiae; Thermodynamics

Chemical Name: Fungal Proteins; RNA, mitochondrial; RNA-Binding Proteins; *Recombinant* Proteins; Ribonucleoproteins; Saccharomyces cerevisiae Proteins; RNA; Magnesium; CBP2 protein, S cerevisiae

3/3,K/10 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10598931 PMID: 8196608

Commitment of yeast pre-mRNA to the splicing pathway requires a novel U1

small nuclear ribonucleoprotein polypeptide, Prp39p.

Lockhart S R; Rymond B C

T. H. Morgan School of Biological Sciences, University of Kentucky, Lexington 40506-0225.

Molecular and cellular biology (UNITED STATES) Jun 1994, 14 (6) p3623-33, ISSN 0270-7306 Journal Code: 8109087

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The binding of a U1 small nuclear ribonucleoprotein (snRNP) particle to the 5' splice site region of a pre-mRNA is a primary step of *intron* recognition. In this report, we identify a novel 75-kDa polypeptide of Saccharomyces cerevisiae, Prp39p, necessary for the *stable* interaction of mRNA precursors with the snRNP components of the pre-mRNA splicing machinery. In vivo, temperature inactivation or metabolic depletion of Prp39p blocks pre-mRNA splicing and causes growth arrest. Analyses of cell extracts reveal a specific and dramatic *increase* in the electrophoretic mobility of the U1 snRNP particle upon Prp39p depletion and demonstrate that extracts deficient in Prp39p activity are unable to form either...

... the U1 snRNP into splicing complexes. On the basis of these and related observations, we propose that Prp39p functions, at least in part, prior to *stable* branch point recognition by the U1 snRNP particle to facilitate or *stabilize* the U1 snRNP/5' splice site interaction.

; Amino Acid Sequence; Base Sequence; DNA Primers; Genes, Fungal; Molecular Sequence Data; Mutagenesis, Insertional; Polymerase Chain Reaction; RNA, Fungal--biosynthesis--BI; *Recombinant* Fusion Proteins --biosynthesis--BI; *Recombinant* Fusion Proteins--metabolism--ME; Regulatory Sequences, *Nucleic* Acid; Saccharomyces cerevisiae--genetics --GE

Chemical Name: DNA Primers; Prp39 protein, S cerevisiae; RNA Precursors; RNA, Fungal; *Recombinant* Fusion Proteins; Ribonucleoprotein, U1 Small Nuclear; Saccharomyces cerevisiae Proteins

3/3,K/11 (Item 8 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10159840 PMID: 1301382

The cloning of the human follicle stimulating hormone receptor and its expression in COS-7, CHO, and Y-1 cells.

Kelton C A; Cheng S V; Nugent N P; Schweickhardt R L; Rosenthal J L; Overton S A; Wands G D; Kuzeja J B; Luchette C A; Chappel S C

Ares Advanced Technology, Inc., Randolph, MA 02368.

Molecular and cellular endocrinology (NETHERLANDS) Nov 1992, 89 (1-2) p141-51, ISSN 0303-7207 Journal Code: 7500844

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

...length human FSH receptor cDNA was engineered for expression in COS-7, CHO, and Y-1 cells. In transient transfections of COS-7 cells and *stable* transfections of Y-1 cells, efficient FSH receptor mRNA accumulation and

isolation of FSH-responsive cell lines occurred only when an *intron* was included in the 5' untranslated region of the FSH receptor transcription unit. Y-1 cells stably transfected with the FSH receptor responded to FSH treatment by rounding up and by synthesizing *increased* amounts of progesterone. Stably transfected CHO cell lines, which responded to FSH by synthesizing *increased* amounts of cAMP, were isolated irrespective of the presence of the heterologous *intron*. The FSH-responsive CHO and Y-1 cell lines may be suitable for the development of better in vitro FSH bioassays. These cells also constitute...

...; metabolism--ME; Gene Expression Regulation; Gene Library; Hamsters; Humans; Introns; Mice; Molecular Sequence Data; Ovary--chemistry--CH; Progesterone--biosynthesis--BI; Rats; Receptors, FSH--biosynthesis--BI; *Recombinant* Fusion Proteins--biosynthesis--BI; Sequence Alignment; Sequence Homology, *Nucleic* Acid; Sertoli Cells--chemistry--CH; Transfection; Tumor Cells, Cultured; Variation (Genetics)

Chemical Name: Receptors, FSH; *Recombinant* Fusion Proteins; Progesterone; DNA

3/3,K/12 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08816281 PMID: 2512291

Immunoglobulin kappa gene expression after *stable* integration. II. Role of the *intronic* MAR and *enhancer* in transgenic mice.

Xu M; Hammer R E; Blasquez V C; Jones S L; Garrard W T

Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas 75235.

Journal of biological chemistry (UNITED STATES) Dec 15 1989, 264 (35) p21190-5, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: GM22201; GM; NIGMS; GM29935; GM; NIGMS; GM31689; GM; NIGMS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Immunoglobulin kappa gene expression after *stable* integration. II. Role of the *intronic* MAR and *enhancer* in transgenic mice.

; Animals; Cell Line; DNA, *Recombinant*--metabolism--ME; Lymphocytes --immunology--IM; Mice; Mice, Inbred Strains; Mice, Transgenic; *Nucleic* Acid Hybridization; Plasmacytoma; RNA, Messenger --isolation and purification--IP; Spleen--immunology--IM; Transcription, Genetic

Chemical Name: DNA, *Recombinant*; Immunoglobulins, kappa-Chain; RNA, Messenger

3/3,K/13 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08212539 PMID: 3346258

The molecular basis for a cytosolic malic enzyme null mutation. Malic enzyme mRNA from MOD-1 null mice contains an internal in-frame duplication that extends the coding sequence by 522 nucleotides.

Brown M L; Wise L S; Rubin C S

Department of Molecular Pharmacology, Atran Laboratories, Albert Einstein

College of Medicine, Bronx, New York 10461.
Journal of biological chemistry (UNITED STATES) Mar 25 1988, 263 (9) p4494-9, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: 5T32-GM07260; GM; NIGMS; AM27165; AM; NIADDK
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...1 null mutation, a lambda gt11 cDNA library was constructed using mRNA from the livers of induced MOD-1 null mice as a template. A *recombinant* phage with a 2-kb insert was isolated by screening with wild type malic enzyme cDNA probes. The subcloned insert exhibited an atypical (non-wild... ... 262, 1558-1565). An open reading frame is retained throughout the duplicated sequence. The discovery of a 522-nucleotide in-frame duplication accounts for the *increased* size of MOD-1 null malic enzyme mRNAs and suggests that a variant malic enzyme polypeptide that is 19 kDa larger than the wild type...

... abnormal junction between the reiterated sequences hybridized with the 2.5 and 3.6-kb MOD-1 null malic enzyme mRNAs but failed to form *stable* complexes with wild type malic enzyme mRNAs. Thus, both MOD-1 null malic enzyme mRNAs contain the duplication deduced from cDNA sequence analyses. The MOD-1 null mutation might originate from an unequal crossover between homologous regions of two different *introns* in the malic enzyme gene, thereby causing the duplication of one or more exons.
; Animals; Base Sequence; Cytosol--enzymology--EN; DNA--analysis--AN; Mice; Molecular Sequence Data; *Nucleic* Acid Hybridization

3/3,K/14 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

1969-2005/Oct W4
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Set	Items	Description
S1	2511	INTRON? (S) (STABLE OR STABILI?) (S) (INCREAS? OR ENHANC?)
S2	55	S1 AND RECOMBINANT? AND NUCLEIC
S3	47	RD (unique items)

>>>KWIC option is not available in file(s): 399

3/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011894725 BIOSIS NO.: 199900154385
Fibroblast growth factor-8 expression is regulated by intronic engrailed and Pbx1-binding sites
AUTHOR: Gemel Joanna; Jacobsen Christina; Macarthur Craig A (Reprint)
AUTHOR ADDRESS: Washington Univ. Sch. Med., Dep. Pediatr., Campus Box 8116, One Children's Place, St. Louis, MO 63110, USA**USA
JOURNAL: Journal of Biological Chemistry 274 (9): p6020-6026 Feb. 26, 1999 1999
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: the vertebrate embryo. We now report on the identification of regions of Fgf8 important for its transcriptional regulation in murine ES cell-derived embryoid bodies. *Stable* transfection of ES cells, using a human growth hormone reporter gene, was employed to identify regions of the Fgf8 gene with promoter/*enhancer* activity. A 2-kilobase 5' region of Fgf8 was shown to contain promoter activity. A 0.8-kilobase fragment derived from the large *intron* of Fgf8 was found to *enhance* human growth hormone expressed from the Fgf8 promoter 3-4-fold in an orientation dependent manner. The *intronic* fragment contains DNA-binding sites for the AP2, Pbx1, and Engrailed transcription factors. Gel shift and Western blot experiments documented the presence of these transcription...

...nuclear extracts from ES cell embryoid bodies. In vitro mutagenesis of the Engrailed or Pbx1 site demonstrated that these sites modulate the activity of the *intronic* fragment. In addition, in vitro mutagenesis of both Engrailed and Pbx1 sites indicated that other unidentified sites are responsible for the transcriptional *enhancement* observed with the *intronic* fragment.
DESCRIPTORS:
...METHODS & EQUIPMENT: analytical method, *nucleic* acid labeling...

...*Recombinant* DNA Technology, genetic engineering method...

...*Recombinant* DNA Technology, sequencing techniques, sequencing method

3/3,K/2 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

02403637 2003186510
Novel functional role of CA repeats and hnRNP L in RNA stability
Hui J.; Reither G.; Bindereif A.
ADDRESS: A. Bindereif, Institut fur Biochemie, Justus-Liebig-Universitat Giessen, Heinrich-Buff-Ring 58, D-35392 Giessen, Germany
EMAIL: albrecht.bindereif@chemie.bio.uni-giessen.de
Journal: RNA, 9/8 (931-936), 2003, United States
PUBLICATION DATE: August 1, 2003
CODEN: RNARF
ISSN: 1355-8382
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 15

CA dinucleotide repeat sequences are very common in the human genome. We have recently demonstrated that the polymorphic CA repeats in *intron* 13 of the human endothelial nitric oxide synthase (eNOS) gene function as an unusual, length-dependent splicing *enhancer*. The CA repeat *enhancer* requires for its activity specific binding of hnRNP L. Here we show that in the absence of bound hnRNP L, the pre-mRNA is cleaved directly upstream of the CA repeats. The addition of *recombinant* hnRNP L restores RNA *stability*. CA repeats are both necessary and sufficient for this specific cleavage in the 5prime adjacent RNA sequence. We conclude that - in addition to its role...

CLASSIFICATION CODE AND DESCRIPTION:
...*Nucleic* Acid Structure and Biophysics

3/3,K/3 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

04004118 H.W. WILSON RECORD NUMBER: BGSI99004118 (USE FORMAT 7 FOR FULLTEXT)
Alternative splicing of pre-mRNA: developmental consequences and mechanisms of regulation.
Lopez, A. Javier
Annual Review of Genetics (Annu Rev Genet) v. 32 ('98) p. 279-305
SPECIAL FEATURES: bibl il ISSN: 0066-4197
LANGUAGE: English

COUNTRY OF PUBLICATION: United States
WORD COUNT: 13032

(USE FORMAT 7 FOR FULLTEXT)

TEXT:
... stabilize binding of U2AF to the RNA or form a bridge to U1 snRNP at the 5' splice site (72, 143, 149; but see 103).

ENHANCEMENT OF SPLICE SITE RECOGNITION
Recognition of a particular splice ...site can be ensured by a strong match to the consensus sequence or by the assistance of cis-acting elements and transacting factors. Across short *introns*, U1 snRNP at the 5' splice site and U2AF at the polypyrimidine tract can interact through extrinsic factors to *stabilize* binding and juxtapose the splice sites in a commitment complex (reviewed in 14, 99). When internal exons are flanked by longer *introns*, interactions can occur across the exon to *stabilize* the binding of U2AF and U1 snRNP (reviewed in 9, 14). These exon bridging interactions are limited to exons between 50 and 500 nt long...

...is too large for effective interaction. When the distances between splice sites are not propitious, or when a splice site is inherently weak, cis-acting *enhancers* can help recruit the essential splicing factors (14, 22). Splicing *enhancers* can be position-dependent; most are located close to the splice site that they activate, and changing their location can alter their dependence on particular...binds to a poly(U) run in the polypyrimidine tract of the regulated 3' splice site (67, 111, 121, 135), and in vitro experiments with *recombinant* proteins show that binding of SXL precludes binding by U2AF (135). If the RS domain of U2AF65 is attached to SXL, however, SXL is transformed...

...cases has also been attributed to reduced access of U2AF to the polypyrimidine tract because binding competition can be demonstrated in vitro and preincubation with *recombinant* U2AF counteracts the PTB-dependent inhibition (26, 76, 121). However, it is not clear whether PTB functions in vivo as an alternative splicing factor or...required for effective repression of IVS3 splicing (56).

What, if any, is the role of U1 snRNP in the repressor complex? It may help to *stabilize* the complex, whose principal function may be to block access to the authentic 5' splice site. U1 snRNP may itself hinder access to this splice...

...to serve a regulatory role. Recruitment of U1 snRNP to regulatory elements also occurs in other systems. U1 snRNP associates with some vertebrate exonic splicing *enhancers* (123, 142) and with a 5' splice site consensus sequence within an *intronic* element that stimulates a regulated cleavage/polyadenylation site in the pre-mRNA for calcitonin/calcitonin gene-related peptide (CT/CGRP) (81). Although the functional significance is not known in the former cases, *enhancement* of in vitro poly-adenylation in the CT/CGRP RNA requires U1 RNA. The involvement of PSI in recruiting U1 snRNP to the F1 pseudo...

...splicing factors, on the other. Substantial experimental and correlational evidence has implicated SR proteins as dose-dependent positive regulators that influence alternative splicing decisions through *stabilization* of U1 snRNP binding or *enhancer* activation (reviewed in 23, 44, 86, 139). Another example may be the KH domain protein KSRP. Inclusion of the c-src N1 exon requires the cooperative assembly of an

intronic activator complex that depends critically on KSRP; KSRP is enriched in neuronal cells, where N1 is normally included, but it is not restricted to this...DS, Fresco LD, Keene JD. 1992. RNA specificity of a Drosophila snRNP protein that shares sequence homology with mammalian U1-A and U2-B proteins. *Nucleic* Acids Res. 20:3645-50

59. Hedley ML, Maniatis T. 1991. Sex-specific splicing and polyadenylation of dsx pre-mRNA requires a sequence that binds...Sakamoto H, Inoue K, Higuchi I, Ono Y, Shimura Y. 1992. Control of Drosophila Sex-lethal pre-mRNA splicing by its own female-specific product. *Nucleic* Acids Res. 20:5533-40

109. Salz HK. 1992. The genetic analysis of snf: a Drosophila sex determination gene required for activation of Sex-lethal...

3/3,K/4 (Item 1 from file: 155)

18028150 PMID: 15632113

Triticum durum metallothionein. Isolation of the gene and structural characterization of the protein using solution scattering and molecular modeling.

Bilecen Kivanc; Ozturk Umit H; Duru Adil D; Sutlu Tolga; Petoukhov Maxim V; Svergun Dimitri I; Koch Michel H J; Sezerman Ugur O; Cakmak Ismail; Sayers Zehra

Sabanci University, Faculty of Engineering and Natural Sciences, 34956, Orhanli, Tuzla, Istanbul, Turkey.

Journal of biological chemistry (United States) Apr 8 2005, 280 (14) p13701-11, ISSN 0021-9258 Journal Code: 2985121R

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

A novel gene sequence, with two exons and one *intron*, encoding a metallothionein (MT) has been identified in durum wheat Triticum durum cv. Balcali85 genomic DNA. Multiple alignment analyses on the cDNA and the translated...

... residue-long hinge region devoid of cysteines. dMT was overexpressed in Escherichia coli as a fusion protein (GSTdMT), and bacteria expressing the fusion protein showed *increased* tolerance to cadmium in the growth medium compared with controls. Purified GSTdMT was characterized by SDS- and native-PAGE, size exclusion chromatography, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry. It was shown that the *recombinant* protein binds 4 +/- 1 mol of cadmium/mol of protein and has a high tendency to form *stable* oligomeric structures. The structure of GSTdMT and dMT was investigated by synchrotron x-ray solution scattering and computational methods. X-ray scattering measurements indicated a strong tendency for GSTdMT to form dimers and trimers in solution and yielded structural models that were compatible with a *stable* dimeric form in which dMT had an extended conformation. Results of homology modeling and ab initio solution scattering approaches produced an elongated dMT structure with...

...; chemistry--CH; Metallothionein--genetics--GE; Metallothionein --metabolism--ME; Models, Molecular; Molecular Sequence Data; Plant Proteins--chemistry--CH; Plant Proteins--genetics--GE; Plant Proteins --metabolism--ME; *Recombinant* Fusion Proteins--chemistry--CH; *Recombinant* Fusion Proteins--genetics--GE; *Recombinant* Fusion Proteins

--metabolism--ME; Sequence Alignment; Sequence Homology, *Nucleic* Acid
Chemical Name: Plant Proteins; *Recombinant* Fusion Proteins; Cadmium; Metallothionein

3/3,K/5 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15018324 PMID: 14561886
The roles of endonucleolytic cleavage and exonucleolytic digestion in the 5'-end processing of S. cerevisiae box C/D snoRNAs.
Lee Chrissie Young; Lee Albert; Chanfreau Guillaume
Department of Chemistry and Biochemistry and the Molecular Biology Institute, University of California Los Angeles, Los Angeles, California 90095-1569, USA.
RNA (New York, N.Y.) (United States) Nov 2003, 9 (11) p1362-70, ISSN 1355-8382 Journal Code: 9509184
Contract/Grant No.: GM07185; GM; NIGMS; GM0896; GM; NIGMS; R01-GM61518; GM; NIGMS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Small nucleolar RNAs (snoRNAs) play important roles in ribosomal RNA metabolism. In Saccharomyces cerevisiae, box C/D snoRNAs are synthesized from excised *introns* , polycistronic precursors, or independent transcription units. Previous studies have shown that only a few independently transcribed box C/D snoRNAs are processed at their 5...

... were identified in vivo when the 5' --> 3' exonucleases Xrn1p and Rat1p are inactivated (xrn1delta rat1-1) and in vitro using model RNA substrates and *recombinant* Rnt1p. Some of these snoRNAs show *increased* levels of unprocessed precursors when the rnt1Delta deletion is combined to the xrn1delta rat1-1 mutation, suggesting that these exonucleases participate in the 5' processing...

...Unprocessed precursors are not significantly destabilized in the absence of the trimethylguanosine capping enzyme Tgs1p, suggesting that a 5' monomethyl cap is sufficient to ensure *stabilization* of these precursors. These results demonstrate that the majority of independently transcribed box C/D snoRNAs from the yeast genome undergo 5'-end processing and...
; Base Sequence; Hydrolysis; Molecular Sequence Data; *Nucleic* Acid Conformation; RNA, Fungal--chemistry--CH; RNA, Small Nucleolar--chemistry --CH; *Recombinant* Proteins--metabolism--ME
Chemical Name: RNA, Fungal; RNA, Small Nucleolar; *Recombinant* Proteins; Endonucleases; Exonucleases

3/3,K/6 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13944811 PMID: 11698502
A highly conserved c-fms gene intronic element controls macrophage-specific and regulated expression.
Himes S R; Tagoh H; Goonetilleke N; Sasmono T; Oceandy D; Clark R;

Bonifer C; Hume D A
Institute for Molecular Bioscience, University of Queensland, Brisbane 4072, Australia.
Journal of leukocyte biology (United States) Nov 2001, 70 (5) p812-20, ISSN 0741-5400 Journal Code: 8405628
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... encodes the receptor for macrophage colony-stimulating factor-1. This gene is expressed selectively in the macrophage cell lineage. Previous studies have implicated sequences in *intron* 2 that control transcript elongation in tissue-specific and regulated expression of c-fms. Four macrophage-specific deoxyribonuclease I (DNase I)-hypersensitive sites (DHSs) were identified within mouse *intron* 2. Sequences of these DHSs were found to be highly conserved compared with those in the human gene. A 250-bp region we refer to as the fms *intronic* regulatory element (FIRE), which is even more highly conserved than the c-fms proximal promoter, contains many consensus binding sites for macrophage-expressed transcription factors including Sp1, PU.1, and C/EBP. FIRE was found to act as a macrophage-specific *enhancer* and as a promoter with an antisense orientation preference in transient transfections. In *stable* transfections of the macrophage line RAW264, as well as in clones selected for high- and low-level c-fms mRNA expression, the presence of *intron* 2 *increased* the frequency and level of expression of reporter genes compared with those attained using the promoter alone. Removal of FIRE abolished reporter gene expression, revealing a suppressive activity in the remaining *intronic* sequences. Hence, FIRE is shown to be a key regulatory element in the fms gene.

...; Genes, Reporter; Humans; Luciferases--biosynthesis--BI; Luciferases --genetics--GE; Mice; Molecular Sequence Data; Oligodeoxyribonucleotides, Antisense--genetics--GE; Oligonucleotide Array Sequence Analysis; RNA, Messenger--biosynthesis--BI; *Recombinant* Fusion Proteins--biosynthesis --BI; Regulatory Sequences, *Nucleic* Acid; Sequence Alignment; Sequence Homology, *Nucleic* Acid; Transcription Factors--metabolism--ME; Transfection

Chemical Name: Oligodeoxyribonucleotides, Antisense; RNA, Messenger; *Recombinant* Fusion Proteins; Transcription Factors; Luciferases; Receptor, Macrophage Colony-Stimulating Factor; Deoxyribonuclease I

3/3,K/7 (Item 4 from file: 155)

12610594 PMID: 10410675

A role for RNA processing in regulating expression from transfected genes.

McBurney M W; Yang X; Jardine K; Cormier M
Ottawa Regional Cancer Center, University of Ottawa, Canada. michael mcburney@cancercare.on.ca

Somatic cell and molecular genetics (UNITED STATES) Jul 1998, 24 (4) p203-15, ISSN 0740-7750 Journal Code: 8403568
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM

Record type: MEDLINE; Completed

We have examined the expression of cloned genes following their *stable* integration into the genome of pluripotent embryonal carcinoma stem cells. Transfected genes integrate into the genome as tandem arrays. Expression of reporter genes from these...

... in embryonal carcinoma cells is inefficient probably because genes are subject to repeat-induced gene silencing. We found that expression of reporter genes was significantly *enhanced* if co-transfected with cloned fragments derived from the murine Pgk-1 gene. The *enhanced* expression required (a) that the Pgk-1 fragment carries an active promoter, (b) that the promoter drives transcription through a region of more than 12 kbp, and (c) that this transcribed region contains both *introns* and exons. Reporter gene activity did not require specific Pgk-1 DNA sequences suggesting that the coupled processes of transcription and RNA processing conferred activity...

...; and inhibitors--AI; Histone Deacetylases--metabolism--ME; Introns --genetics--GE; Lac Operon--genetics--GE; Mice; Phosphoglycerate Kinase --metabolism--ME; Plasmids--genetics--GE; Promoter Regions (Genetics); *Recombinant* Fusion Proteins--drug effects--DE; *Recombinant* Fusion Proteins--genetics--GE; *Recombinant* Fusion Proteins--metabolism--ME; Recombination, Genetic; Repetitive Sequences, *Nucleic* Acid; Transcription, Genetic; Transfection; Tumor Cells, Cultured; beta-Galactosidase--drug effects--DE; beta-Galactosidase--genetics--GE; beta-Galactosidase--metabolism--ME

Chemical Name: Butyrates; Plasmids; *Recombinant* Fusion Proteins; Phosphoglycerate Kinase; beta-Galactosidase; Histone Deacetylases

3/3,K/8 (Item 5 from file: 155)

11634153 PMID: 8945637

Human kinesin light (beta) chain gene: DNA sequence and functional characterization of its promoter and first exon.

Chernajovsky Y; Brown A; Clark J

Kennedy Institute of Rheumatology, Molecular Biology Laboratory, Hammersmith, London, UK.

DNA and cell biology (UNITED STATES) Nov 1996, 15 (11) p965-74, ISSN 1044-5498 Journal Code: 9004522

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... system, producing a 70-kDa protein. Using this cDNA as a probe, we isolated and sequenced the promoter, first exon, and part of the first *intron* of this gene from a genomic lambda EMBL3 human placental DNA library. The whole gene spans more than 90 kb. The beta kinesin promoter region...

... of beta kinesin was 75-fold more active than the HSV-tk promoter. The first exon contains the 5'-untranslated sequence capable of forming a *stable* double-hairpin loop, which functions as a translational *enhancer* . Its deletion decreases the efficiency of in vitro translation of beta kinesin mRNA and confers *increased* translation to a CAT reporter gene.

...; Cell Line; Cell-Free System; Chloramphenicol O-Acetyltransferase --biosynthesis--BI; Dogs; Gene Library; Hela Cells; Humans; Macromolecular Substances; Microsomes--metabolism--ME; Molecular Sequence Data; Neuroblastoma; *Nucleic* Acid Conformation; Open Reading Frames; Pancreas --metabolism--ME; Placenta--metabolism--ME; Pregnancy; Protein Biosynthesis ; Protein Processing, Post-Translational; RNA, Messenger--chemistry--CH; RNA, Messenger--metabolism--ME; *Recombinant* Fusion Proteins --biosynthesis--BI; Transcription, Genetic; Transfection

Chemical Name: Macromolecular Substances; RNA, Messenger; *Recombinant* Fusion Proteins; Chloramphenicol O-Acetyltransferase; Kinesin

3/3,K/9 (Item 6 from file: 155)

10999590 PMID: 7540041

Efficient protein-facilitated splicing of the yeast mitochondrial bI5 intron.

Weeks K M; Cech T R

Department of Chemistry and Biochemistry, Howard Hughes Medical Institute, University of Colorado, Boulder 80309-0215, USA.

Biochemistry (UNITED STATES) Jun 13 1995, 34 (23) p7728-38, ISSN 0006-2960 Journal Code: 0370623

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The splicing factor CBP2 is required to excise the yeast mitochondrial group I *intron* bI5 in vivo and at low magnesium ion concentrations in vitro. CBP2 binding is strengthened 20-fold by *increasing* Mg2+ concentrations from 5 to 40 mM, implying the protein binds, in part, to the same structure as that *stabilized* by the cation. The same transition is also observed as a cooperative *increase* in the rate of self-processing between 5 and 40 mM Mg2+, providing strong evidence for an RNA folding transition promoted by either Mg2+ or...

... evidence that kcat is limited by chemistry at low pH and by a conformational step at high pH. Because binding by either Mg2+ or CBP2 *increases* the rate of chemistry more than the rate of the conformational step, in the physiological pH range (7-7.6) the protein-facilitated reaction is...

; Base Sequence; Hydrogen Bonding; Introns; Kinetics; Magnesium --metabolism--ME; Molecular Sequence Data; *Nucleic* Acid Conformation; RNA-Binding Proteins--chemistry--CH; *Recombinant* Proteins; Saccharomyces cerevisiae; Thermodynamics

Chemical Name: Fungal Proteins; RNA, mitochondrial; RNA-Binding Proteins; *Recombinant* Proteins; Ribonucleoproteins; Saccharomyces cerevisiae Proteins; RNA; Magnesium; CBP2 protein, S cerevisiae

3/3,K/10 (Item 7 from file: 155)

10598931 PMID: 8196608

Commitment of yeast pre-mRNA to the splicing pathway requires a novel U1

small nuclear ribonucleoprotein polypeptide, Prp39p.
Lockhart S R; Rymond B C
T. H. Morgan School of Biological Sciences, University of Kentucky, Lexington 40506-0225.
Molecular and cellular biology (UNITED STATES) Jun 1994, 14 (6) p3623-33, ISSN 0270-7306 Journal Code: 8109087
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The binding of a U1 small nuclear ribonucleoprotein (snRNP) particle to the 5' splice site region of a pre-mRNA is a primary step of *intron* recognition. In this report, we identify a novel 75-kDa polypeptide of Saccharomyces cerevisiae, Prp39p, necessary for the *stable* interaction of mRNA precursors with the snRNP components of the pre-mRNA splicing machinery. In vivo, temperature inactivation or metabolic depletion of Prp39p blocks pre-mRNA splicing and causes growth arrest. Analyses of cell extracts reveal a specific and dramatic *increase* in the electrophoretic mobility of the U1 snRNP particle upon Prp39p depletion and demonstrate that extracts deficient in Prp39p activity are unable to form either...

... the U1 snRNP into splicing complexes. On the basis of these and related observations, we propose that Prp39p functions, at least in part, prior to *stable* branch point recognition by the U1 snRNP particle to facilitate or *stabilize* the U1 snRNP/5' splice site interaction.
; Amino Acid Sequence; Base Sequence; DNA Primers; Genes, Fungal; Molecular Sequence Data; Mutagenesis, Insertional; Polymerase Chain Reaction; RNA, Fungal--biosynthesis--BI; *Recombinant* Fusion Proteins --biosynthesis--BI; *Recombinant* Fusion Proteins--metabolism--ME; Regulatory Sequences, *Nucleic* Acid; Saccharomyces cerevisiae--genetics --GE
Chemical Name: DNA Primers; Prp39 protein, S cerevisiae; RNA Precursors; RNA, Fungal; *Recombinant* Fusion Proteins; Ribonucleoprotein, U1 Small Nuclear; Saccharomyces cerevisiae Proteins

3/3,K/11 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10159840 PMID: 1301382
The cloning of the human follicle stimulating hormone receptor and its expression in COS-7, CHO, and Y-1 cells.
Kelton C A; Cheng S V; Nugent N P; Schweickhardt R L; Rosenthal J L; Overton S A; Wands G D; Kuzeja J B; Luchette C A; Chappel S C
Ares Advanced Technology, Inc., Randolph, MA 02368.
Molecular and cellular endocrinology (NETHERLANDS) Nov 1992, 89 (1-2) p141-51, ISSN 0303-7207 Journal Code: 7500844
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...length human FSH receptor cDNA was engineered for expression in COS-7, CHO, and Y-1 cells. In transient transfections of COS-7 cells and *stable* transfections of Y-1 cells, efficient FSH receptor mRNA accumulation and

isolation of FSH-responsive cell lines occurred only when an *intron* was included in the 5' untranslated region of the FSH receptor transcription unit. Y-1 cells stably transfected with the FSH receptor responded to FSH treatment by rounding up and by synthesizing *increased* amounts of progesterone. Stably transfected CHO cell lines, which responded to FSH by synthesizing *increased* amounts of cAMP, were isolated irrespective of the presence of the heterologous *intron*. The FSH-responsive CHO and Y-1 cell lines may be suitable for the development of better in vitro FSH bioassays. These cells also constitute...

...; metabolism--ME; Gene Expression Regulation; Gene Library; Hamsters; Humans; Introns; Mice; Molecular Sequence Data; Ovary--chemistry--CH; Progesterone--biosynthesis--BI; Rats; Receptors, FSH--biosynthesis--BI; *Recombinant* Fusion Proteins--biosynthesis--BI; Sequence Alignment; Sequence Homology, *Nucleic* Acid; Sertoli Cells--chemistry--CH; Transfection; Tumor Cells, Cultured; Variation (Genetics)

Chemical Name: Receptors, FSH; *Recombinant* Fusion Proteins; Progesterone; DNA

3/3,K/12 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08816281 PMID: 2512291

Immunoglobulin kappa gene expression after *stable* integration. II. Role of the *intronic* MAR and *enhancer* in transgenic mice.

Xu M; Hammer R E; Blasquez V C; Jones S L; Garrard W T

Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas 75235.

Journal of biological chemistry (UNITED STATES) Dec 15 1989, 264 (35) p21190-5, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: GM22201; GM; NIGMS; GM29935; GM; NIGMS; GM31689; GM; NIGMS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Immunoglobulin kappa gene expression after *stable* integration. II. Role of the *intronic* MAR and *enhancer* in transgenic mice.

; Animals; Cell Line; DNA, *Recombinant*--metabolism--ME; Lymphocytes --immunology--IM; Mice; Mice, Inbred Strains; Mice, Transgenic; *Nucleic* Acid Hybridization; Plasmacytoma; RNA, Messenger --isolation and purification--IP; Spleen--immunology--IM; Transcription, Genetic

Chemical Name: DNA, *Recombinant*; Immunoglobulins, kappa-Chain; RNA, Messenger

3/3,K/13 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08212539 PMID: 3346258

The molecular basis for a cytosolic malic enzyme null mutation. Malic enzyme mRNA from MOD-1 null mice contains an internal in-frame duplication that extends the coding sequence by 522 nucleotides.

Brown M L; Wise L S; Rubin C S

Department of Molecular Pharmacology, Atran Laboratories, Albert Einstein

College of Medicine, Bronx, New York 10461.
Journal of biological chemistry (UNITED STATES) Mar 25 1988, 263 (9) p4494-9, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: 5T32-GM07260; GM; NIGMS; AM27165; AM; NIADDK
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

...1 null mutation, a lambda gt11 cDNA library was constructed using mRNA from the livers of induced MOD-1 null mice as a template. A *recombinant* phage with a 2-kb insert was isolated by screening with wild type malic enzyme cDNA probes. The subcloned insert exhibited an atypical (non-wild... ... 262, 1558-1565). An open reading frame is retained throughout the duplicated sequence. The discovery of a 522-nucleotide in-frame duplication accounts for the *increased* size of MOD-1 null malic enzyme mRNAs and suggests that a variant malic enzyme polypeptide that is 19 kDa larger than the wild type...

... abnormal junction between the reiterated sequences hybridized with the 2.5 and 3.6-kb MOD-1 null malic enzyme mRNAs but failed to form *stable* complexes with wild type malic enzyme mRNAs. Thus, both MOD-1 null malic enzyme mRNAs contain the duplication deduced from cDNA sequence analyses. The MOD-1 null mutation might originate from an unequal crossover between homologous regions of two different *introns* in the malic enzyme gene, thereby causing the duplication of one or more exons.
; Animals; Base Sequence; Cytosol--enzymology--EN; DNA--analysis--AN; Mice; Molecular Sequence Data; *Nucleic* Acid Hybridization

3/3,K/14 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0378931 DBR Accession No.: 2005-24637 PATENT
Producing plasminogen, useful for producing a polypeptide having protease activity, comprises culturing a duckweed plant, plant cell or nodule - production of *recombinant* plasminogen in a duckweed plant useful for the the production of a protease
AUTHOR: SPENCER D; DICKEY L F; GASDASKA J R; WANG X; COX K M; PEELE C G
PATENT ASSIGNEE: BIOLEX INC 2005
PATENT NUMBER: WO 200578109 PATENT DATE: 20050825 WPI ACCESSION NO.: 2005-571610 (200558)
PRIORITY APPLIC. NO.: US 543487 APPLIC. DATE: 20040211
NATIONAL APPLIC. NO.: WO 2005US4245 APPLIC. DATE: 20050211
LANGUAGE: English

Producing plasminogen, useful for producing a polypeptide having protease activity, comprises culturing a duckweed plant, plant cell or nodule - production of *recombinant* plasminogen in a duckweed plant useful for the the production of a protease
...ABSTRACT: culturing a duckweed plant or duckweed plant cell or nodule, where the duckweed plant or duckweed plant cell or nodule is stably transformed with a *nucleic* acid molecule comprising a nucleotide sequence encoding plasminogen, plasminogen fragment or microplasminogen and an operably linked coding sequence for a signal peptide that directs secretion...

... duckweed plant, duckweed plant cell or nodule or duckweed culture medium. INDEPENDENT CLAIMS are also included for: (1) an improvement in a method of producing *stable* plasminogen comprises producing the plasminogen; (2) a stably transformed duckweed plant, duckweed plant cell, or duckweed nodule, where the duckweed comprises a DNA construct containing...

... plasminogen, and a transcriptional termination sequence, where the leader sequence, the promoter sequence and the termination sequence all function in duckweed; and (3) an isolated *nucleic* acid molecule comprising a nucleotide sequence encoding an amino acid sequence selected from: (i) a sequence of 791 amino acids (SEQ ID NO: 4), given ...

... plasminogen fragment or microplasminogen; (b) duckweed-preferred codons in the coding sequence for the signal peptide; (c) an operably linked nucleotide sequence comprising a plant *intron* that is inserted upstream of the coding sequence for microplasminogen; or (d) an operably linked nucleotide sequence comprising a leader sequence that *increases* the translation of the nucleotide sequence encoding plasminogen or plasminogen fragment, where the nucleotide sequence encoding plasminogen, plasminogen fragment or signal peptide comprises 70-100 % duckweed-preferred codons. The plant *intron* is derived from the maize alcohol dehydrogenase 1 gene, where the plant *intron* consists essentially of a sequence of 554 base pairs (bp; SEQ ID NO: 1), given in the specification. The plasminogen fragment comprises at least 80...

DESCRIPTORS: *recombinant* plasminogen prep., isol., purification, expression in duckweed, appl., protease prep. blood-clotting protein plant enzyme DNA sequence protein sequence (24, 40)

3/3,K/15 (Item 2 from file: 357)

0360924 DBR Accession No.: 2005-06628 PATENT

New purified RNA processing protein complexes with tRNA splicing endonuclease or pre-ribosomal cleavage activity, useful for diagnosing, preventing or treating wounds, cancer and neoplastic diseases - involving vector-mediated gene transfer and expression in host cell for gene therapy

AUTHOR: TROTTA C R; PAUSHKIN S
PATENT ASSIGNEE: PTC THERAPEUTICS INC 2005
PATENT NUMBER: WO 200503316 PATENT DATE: 20050113 WPI ACCESSION NO.: 2005-112398 (200512)
PRIORITY APPLIC. NO.: US 484615 APPLIC. DATE: 20030702
NATIONAL APPLIC. NO.: WO 2004US21334 APPLIC. DATE: 20040702
LANGUAGE: English

...ABSTRACT: protein complex is new. DETAILED DESCRIPTION - A purified human protein complex cited above comprises: (a) Sen2 (ACCESSION NO: NP079541), or a protein encoded by a *nucleic* acid that hybridizes to the Sen2 encoding *nucleic* acid (ACCESSION NO: NM025265) or its complement under high stringency conditions; (b) Sen15 or a protein encoded by a *nucleic* acid that hybridizes to the Sen15 encoding *nucleic* acid (ACCESSION NO: NM052965) or its complement under high stringency conditions; (c) Sen34 (ACCESSION NO: NP076980), or a protein

encoded by a *nucleic* acid that hybridizes to the Sen34 encoding *nucleic* acid (ACCESSION NO: NM024075) or its complement under high stringency conditions; or (d) Sen54 (ACCESSION NO: XP208944), or a protein encoded by a *nucleic* acid that hybridizes to the Sen54 encoding *nucleic* acid (ACCESSION NO: XM208944) or its complement under high stringency conditions, The high stringency conditions comprise hybridization in a buffer consisting of 6x saline sodium...

... or immunospecifically binds to Sen2, Sen15, Sen34, or Sen54; (2) generating an antibody comprising immunizing an animal with the complex cited above; (3) a purified *nucleic* acid encoding a protein comprising the amino acid sequence of 448 or 1347 base pairs(SEQ ID NO: 12 or 11); (4) a purified *nucleic* acid comprising a contiguous open reading frame which encodes a polypeptide comprising amino acid 280-330 of SEQ ID NO: 12; (5) a purified *nucleic* acid which hybridizes over its full length to the complement of a *nucleic* acid comprising SEQ ID NO: 11 under high stringency conditions, where the high stringency conditions comprise hybridization in a buffer consisting of 6x SSC, 50 ...

... 37 degreesC, and washing in a buffer consisting of 0.1 xSSC, for 45 minutes at 50 degreesC; (6) a vector comprising any of the *nucleic* acids cited above; (7) a host cell comprising the vector of (6) or any of the *nucleic* acids cited; (8) producing a polypeptide comprising culturing the host cell of (7); (9) a purified polypeptide comprising SEQ ID NO: 12, or the amino acid sequence encoded by a *nucleic* acid sequence that hybridizes over its full length to the complement of SEQ ID NO: 11 under high stringency conditions as cited above; (10) an...

... under conditions conducive to formation of a complex comprising the proteins, and determining the amount of the complex;(15) identifying a compound that modulates the *stability* of a complex, comprising incubating the complex cited above in the presence of a compound under conditions conducive to maintaining the complex, and determining the...

... compound that modulates human tRNA splicing endonuclease activity, comprising contacting a member of a library of compounds with a the complex cited above and a *nucleic* acid comprising a reporter gene, where the reporter gene comprises a tRNA *intron*, and where all factors required for gene expression are present, and detecting the expression of the reporter gene; (17) identifying a compound that modulates 3' end pre-mRNA endonuclease cleavage activity, comprising contacting a member of a library of compounds with the complex cited above and a *nucleic* acid comprising a reporter gene and a cleavage site for a 3' end pre-mRNA endonuclease, where the reporter gene is located 3' of the...

... above with the mRNA or pre-mRNA molecule. BIOTECHNOLOGY - Preferred Complex: The complex further comprises Clp1 (ACCESSION NO: NP006822) or a protein encoded by a *nucleic* acid that hybridizes to the Clp1 encoding *nucleic* acid (ACCESSION NO: NM006831) or its complement under high stringency conditions. The complex also comprises one or more of the following: (a) Cleavage-Polyadenylation Specificity Factor or proteins encoded by *nucleic* acids that hybridize to the Cleavage-Polyadenylation Specificity Factor encoding *nucleic* acids or their complements under high stringency conditions; (b) Cleavage Factor Im or proteins encoded by *nucleic* acids that hybridize to the Cleavage Factor Im, encoding *nucleic* acids or their complements under high stringency conditions; (c) Cleavage Factor IIm or proteins encoded by *nucleic* acids that hybridize to the Cleavage Factor IIm encoding

nucleic acids or their complements under high stringency conditions; or (d) Cleavage Stimulation Factor or proteins encoded by *nucleic* acids that hybridize to the Cleavage Stimulation Factor encoding *nucleic* acids or their complements under high stringency conditions. The complex further comprises one or more of the following: (a) CPSF160 or a protein encoded by a *nucleic* acid that hybridizes to CPSF160 encoding *nucleic* acid or its complement under high stringency conditions; (b) CPSF30 or a protein encoded by a *nucleic* acid that hybridizes to CPSF30 encoding *nucleic* acid or its complement under high stringency conditions; (c) CstF64 or a protein encoded by a *nucleic* acid that hybridizes to CstF64 encoding *nucleic* acid or its complement under high stringency conditions; or (d) symplekin or a protein encoded by a *nucleic* acid that hybridizes to symplekin encoding *nucleic* acid or its complement under high stringency conditions. The purified complex additionally comprises Sen2deltaEx8, or a protein encoded by a *nucleic* acid that hybridizes under stringent hybridization conditions to a Sen2deltaEx8 encoding *nucleic* acid. Alternatively, the purified complex further comprises: (a) Sen2deltaEx8 with a fully defined sequence of 465 amino acids (SEQ ID NO: 2), or a protein encoded by a *nucleic* acid that hybridizes to the Sen2deltaEx8 encoding *nucleic* acid with a fully defined sequence of 2373 base pairs (SEQ ID NO: 1) or its complement under high stringency conditions; or (b) Sen54 (ACCESSION NO: XP208944), or a protein encoded by a *nucleic* acid that hybridizes to the Sen54 encoding *nucleic* acid (ACCESSION NO: XM208944) or its complement under high stringency conditions, The high stringency conditions comprise hybridization conditions as cited. The complex also comprises one or more of the following: (a) CPSF160 or a protein encoded by a *nucleic* acid that hybridizes to CPSF160 encoding *nucleic* acid or its complement under high stringency conditions; (b) CPSF30 or a protein encoded by a *nucleic* acid that hybridizes to CPSF30 encoding *nucleic* acid or its complement under high stringency conditions; (c) CstF64 or a protein encoded by a *nucleic* acid that hybridizes to CstF64 encoding *nucleic* acid or its complement under high stringency conditions; or (d) symplekin or a protein encoded by a *nucleic* acid that hybridizes to symplekin encoding *nucleic* acid or its complement under high stringency conditions. At least two proteins of the complex are covalently or non-covalently linked to each other. At...

... The complex comprises at least one fragment of a protein, where the fragment binds to one or more other protein components of the complex. Preferred *Nucleic* Acid: The *nucleic* acid of (5) encodes a polypeptide that has RNA nucleolytic activity, and further comprises a heterologous *nucleic* acid sequence. Preferred Polypeptide: The polypeptide further comprises a heterologous amino acid sequence. Preferred Antibody: The antibody of (10) does not bind to Sen2. Preferred...

... measured by FRET. The cell is engineered to express at least one of the protein components of the complex. Identifying a compound that modulates the *stability* of a complex further comprises comparing the ratio between the formed complex relative to the amount of the individual proteins. The proteins are incubated in...

... the absence of the compound or the presence of a control. The compound is tested for inhibition of human tRNA splicing endonuclease activity. The compound *enhances* tRNA splicing endonuclease activity. The method also comprises determining the structure of the compound. The compound directly binds the complex. Identifying a compound that modulates...

... compound is tested for inhibition of the formation of the complex, and for inhibition of human 3' end pre-mRNA endonuclease activity. The compound also *enhances* 3' end pre-mRNA endonuclease activity. The mRNA in the cleaving method comprises a premature stop codon. The compound in any of the identifying methods...

... from a combinatorial library of compounds comprising peptoids, random biooligomers, diversomers such as hydantoins, benzodiazepines and dipeptides, vinylogous polypeptides, nonpeptidal peptidomimetics, oligocarbamates, peptidyl phosphonates, peptide *nucleic* acid libraries, antibody libraries, carbohydrate libraries, and small organic molecule libraries. ACTIVITY - Vulnerary; Cytostatic. No biological data is given. MECHANISM OF ACTION - Endonuclease-Stimulator; Antisense...

DESCRIPTORS: human *recombinant* protein prep., isol., vector-mediated gene transfer, expression in host cell, antisense, appl., cancer, neoplastic disease, vulnerary diagnosis, prevention, therapy, gene therapy animal mammal tumor...

3/3,K/16 (Item 3 from file: 357)

0355152 DBR Accession No.: 2005-00856 PATENT

Determining a global gene regulatory element profile of cells by identifying *nucleic* acid molecule, *nucleic* acid binding protein, regulatory protein, or co-regulatory protein components comprising the gene regulatory element complexes - cell global gene regulatory element expression profiling for DNA or DNA binding protein identification

AUTHOR: WARREN M E; ADAMS C; LABHART P; BALLIVET M; EGAN B S

PATENT ASSIGNEE: GENPATHWAY INC 2004
PATENT NUMBER: WO 200499382 PATENT DATE: 20041118 WPI ACCESSION NO.: 2004-805120 (200479)
PRIORITY APPLIC. NO.: US 426734 APPLIC. DATE: 20030430
NATIONAL APPLIC. NO.: WO 2004US13664 APPLIC. DATE: 20040429
LANGUAGE: English

Determining a global gene regulatory element profile of cells by identifying *nucleic* acid molecule, *nucleic* acid binding protein, regulatory protein, or co-regulatory protein components comprising the gene regulatory element complexes - cell global gene regulatory element expression profiling for DNA...

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Determining a global gene regulatory element profile of cells comprises identifying one or more of the *nucleic* acid molecule, *nucleic* acid binding protein, regulatory protein, or co-regulatory protein components comprising the gene regulatory element complexes formed to determine the global gene regulatory element profile...

... least one cell or from cellular contents obtained from at least one cell, one or more types of gene regulatory element complexes formed between cellular *nucleic* acid and associated protein components, the complexes comprising: (i) *nucleic* acid molecules and *nucleic* acid binding proteins; (ii) *nucleic* acid binding proteins and regulatory proteins; (iii) *nucleic* acid molecules, *nucleic* acid binding proteins and regulatory proteins; (iv) *nucleic* acid molecules, *nucleic* acid binding proteins, regulatory proteins, and co-regulatory proteins; or (v) its combinations, under conditions conducive to the

formation of the complexes; (b) detecting the components of the complexes that are formed; and (c) identifying one or more of the *nucleic* acid molecule, *nucleic* acid binding protein, regulatory protein, or co-regulatory protein components comprising the complexes to determine a global gene regulatory element profile of the cells or ...

... are produced within at least one cell and isolated from it. They are also produced outside of a cell by contacting a source of cellular *nucleic* acid sequences with a source of cellular proteins to allow for generation of the complexes. The method further comprises identifying transcribed regions regulated by the...

... tissues or portions, cells from organs or portions, or cells from whole organisms or portions. The cells also comprise mixtures of different cell populations. The *nucleic* acid molecules comprise one or more cis sites comprising associated transcribed regions. It also comprises one or more gene regulatory sequences. The *nucleic* acid molecules comprising one or more cis sites are obtained from cells, a preparation of genomic *nucleic* acid molecules, cloned *nucleic* acid sequences, or a library of synthetically prepared *nucleic* acid molecules. Regulatory or co-regulatory proteins are stably associated with the one or more cis sites comprising the *nucleic* acid molecules of the complexes. The *stable* association of the regulatory or co-regulatory proteins and the cis sites comprising the *nucleic* acid molecules of the complexes results from one or more of chemical cross-linking, biological cross-linking, ultraviolet light cross-linking, or cleavable linker interactions. The cross-linking is also reversible. The *nucleic* acid molecule and protein components comprising the complexes are obtained from a total cell extract, a nuclear extract, a cytoplasmic extract, a mitochondrial extract, a...

... gene regulatory element profile for different cells, or two or more populations of cells, and comparing the profiles. It further comprises selecting regulatory protein or *nucleic* acid molecule components of the complexes that bind to molecules involved in gene expression or transcription. The molecules involved in gene expression or transcription comprise transcription factors, promoter-associated factors, or *enhancer* -associated factors. The regulatory proteins detected and identified from the complexes include general transcription factors, specific transcription factors that regulate subsets of genes, transcription-associated...

... or agent and gene expression or regulation of untreated cells. The exogenous substance or agent comprises a drug or chemical. The method further comprises identifying *nucleic* acid regulatory regions in cis site-containing *nucleic* acid molecules comprising the complexes by a method selected from *nucleic* acid amplification, *nucleic* acid sequencing, *nucleic* acid hybridization, or a combination. The method further comprises identifying the *nucleic* acid sequences of the *nucleic* acid molecules bound to protein in the complexes by denaturing the *nucleic* acid sequences comprising the complexes, binding the denatured *nucleic* acid sequences to detectably labeled *nucleic* acid molecules of known sequence, and identifying the *nucleic* acid molecules from the complex that were previously bound to protein by their binding to the detectably labeled *nucleic* acid molecules of known sequence. It further comprises sequencing the identified *nucleic* acid molecules and determining cis site motifs in the identified *nucleic* acid molecules associated with protein in the complexes. The method further comprises quantifying the *nucleic* acid molecules bound to the detectably labeled *nucleic* acid molecules of

known sequence by determining intensity of the detectable label. The detectable label comprises a fluorescent label, a radioactive label, an enzymatic label...

... Array binding is performed by binding the proteins from the complexes onto an array comprising antibodies directed toward the protein in the complex, or binding *nucleic* acid from the complexes onto an array comprising *nucleic* acid molecules of known sequence. Identifying the *nucleic* acid molecules in the isolated complexes optionally comprises cloning fragments of the *nucleic* acid molecules into vectors, and hybridizing the cloned *nucleic* acid molecules to *nucleic* acid probes of known sequence, or sequencing the cloned *nucleic* acid molecules. Analysis of the *nucleic* acid molecules in the isolated complexes comprises amplifying the *nucleic* acid molecules, or fragments, subjecting the amplified *nucleic* acid molecules or fragments to gel electrophoresis and observing amplicons of the expected size or sequences of the expected type. Analysis of the *nucleic* acid molecules in the isolated complexes comprises hybridizing the amplified *nucleic* acid molecules or fragments to macroarrays or microarrays containing known *nucleic* acid sequences. The known *nucleic* acid sequences comprise cis sites, transcription regulatory regions, known transcribed regions, or predicted transcribed regions. Amplifying the *nucleic* acid molecules comprises a method selected from polymerase chain reaction (PCR), quantitative PCR (Q-PCR), ligation-mediated PCR (LM-PCR), transcription-mediated amplification, rolling circle amplification, or ligase chain reaction. The method above further comprises directly sequencing the *nucleic* acid molecules or fragments comprising the complexes, and evaluating the sequences obtained. They are isolated by binding to *nucleic* acid probes of known sequence or to arrays having bound thereto *nucleic* acid probes of known sequence. The isolated *nucleic* acid molecules or fragments are used as templates to synthesize a library of *nucleic* acid fragments comprising a selected population of *nucleic* acid sequences bound to protein in the complexes. The library represents a portion of the bound sequences or sequences that are contiguous to the bound sequences. The *nucleic* acid molecules identified or isolated from the complexes are subjected to subtractive hybridization. Subtractive hybridization results in enriching for *nucleic* acid sequences that are bound by a specific *nucleic* acid binding protein, regulatory protein, or co-regulatory protein in the complex, removing sequences common to regulatory element complexes from two or more different cells...

... to a second compound, cells exposed to an external condition and unexposed cells, or cells exposed to an internal condition and unexposed cells. The complexed *nucleic* acid molecules comprise DNA, RNA, single-stranded DNA, single-stranded RNA, double-stranded DNA, double-stranded RNA, genomic DNA, complementary DNA, DNA complementary to RNA...

... from cellular contents obtained from the cell populations, a plurality of one or more types of gene regulatory element complexes, the complexes formed between cellular *nucleic* acid molecules and associated protein components; (b) detecting the *nucleic* acid molecule or associated protein components of the complexes that are formed; and (c) identifying one or more of the *nucleic* acid molecule or associated protein components comprising the complexes so as to determine a global gene regulatory element profile of the cells or a global...

... from cells, or from cellular contents obtained from the cells, a plurality of one or more types of gene regulatory element complexes formed between cellular *nucleic* acid molecules and associated protein components, the components comprising: (i) *nucleic* acid molecules and *nucleic* acid binding protein complexes, (ii) *nucleic* acid binding protein and regulatory protein complexes, (iii) *nucleic* acid molecules, *nucleic* acid binding protein and regulatory protein complexes, (iv) *nucleic* acid molecules, *nucleic* acid binding protein, regulatory protein and co-regulatory protein complexes, or (v) its combinations, under conditions conducive to the formation of the complexes; (b) isolating one or more of the protein components of the complexes using one or more affinity reagents that bind specifically to: (i) the *nucleic* acid molecule component, (ii) the *nucleic* acid binding protein component, (iii) the regulatory protein component, (iv) the co-regulatory protein component, or (v) its combination; and (c) identifying one or more of the *nucleic* acid molecule components, *nucleic* acid binding protein components, regulatory protein components, or co-regulatory protein components comprising the complexes so as to determine a global gene regulatory element profile ...

... affinity reagents also bind to a general transcription factor, or a specific transcription factor. It also binds to proteins involved in active transcription, or to *nucleic* acid molecules of the complexes. The affinity reagent is selected from *nucleic* acid aptamers or *nucleic* acid probes. The isolated *nucleic* acid molecule components of the complexes are identified by determining their *nucleic* acid sequences or their amino acid sequences, or its combination. The identified *nucleic* acid sequences are further mapped on the appropriate genome using *nucleic* acid sequence databases. The complexes of (a) are formed in solution, on a solid support, in semi-solid medium, in gels, in column matrices, or in polymer formulations. The solution is an aqueous solution, an organic solution, or an inorganic solution. In the method, the *nucleic* acid molecule and associated protein complexes are separated from unbound cellular material. Alternatively, globally profiling gene regulatory activity of cells comprises: (a) obtaining *nucleic* acid molecule and protein complexes formed within cells under conditions conducive to the formation of the complexes, or extracellularly from cellular *nucleic* acids and cellular proteins contacted to allow for production of the complexes; (b) isolating *nucleic* acid molecules from the complexes; (c) enriching the *nucleic* acid molecules for cell-specific transcribed *nucleic* acid molecules; and (d) determining the *nucleic* acid molecules that are specifically transcribed. It further comprises identifying one or more of the proteins that comprise the complexes. The *nucleic* acid comprising the complexes is DNA or RNA. The complexes are obtained using antibodies directed against a protein comprising the complex. The *nucleic* acid is identified by hybridization to *nucleic* acid probes, by binding to specific cis site-containing or regulatory-sequence-containing *nucleic* acid sequences, or by binding to *nucleic* acid molecules of known sequence or to immunoreactive agents arranged in an array. The *nucleic* acid is isolated from the complexes using one or more of protease-digestion, phenol extraction, or ethanol precipitation. The cell-specific transcribed *nucleic* acid is enriched by subtractive hybridization to result in enriching for *nucleic* acid sequences that are bound by a specific *nucleic* acid binding protein, regulatory protein, or co-regulatory protein in the complex, removing sequences common to regulatory element complexes from two or more different cells...

... cell or cell population versus another cell or cell population. Alternatively, globally profiling gene regulatory activity of cells comprises: (a) immunoprecipitating regulatory element complexes comprising *nucleic* acid molecules and bound proteins from one or more cells or populations of cells; (b) analyzing the immunoprecipitated *nucleic* acid molecules for the presence of regulatory regions comprising cis sites or transcribed regions to obtain a global profile of gene regulatory activity; and (c...

...TATA-box binding protein (TBP) and CREB-binding protein (CBP). Analyzing is performed using PCR. The primers in the PCR are specific for promoter sequences, *intronic* sequences, exonic sequences, *enhancer* sequences, sequences 5' to promoter sequences, sequences 5' or 3' to genes or a combination. Analyzing also comprises using quantitative PCR (Q-PCR) to detect transcribed genes. The method further comprises identifying the protein components that are complexed with the *nucleic* acids. Alternatively, globally determining differences in gene regulatory element activity between cells comprises: (a) isolating from a first population of cells a plurality of gene regulatory complexes comprising *nucleic* acid molecule components and associated protein components; (b) analyzing (i) the *nucleic* acid molecule components of the complexes of (a) to determine the presence of cis sites or regulatory regions; (ii) the protein components of the complexes of (a) to identify the proteins as *nucleic* acid binding proteins, regulatory proteins, or co-regulatory proteins; or a combination of (i) and (ii); (c) isolating from a second population of cells of gene regulatory complexes comprising *nucleic* acid molecule components and associated protein components; (d) analyzing (i) the *nucleic* acid molecule components of the complexes of (c) to determine the presence of cis sites or regulatory regions; (ii) the protein components of the complexes of (c) to identify the proteins as *nucleic* acid binding proteins, regulatory proteins, or co-regulatory proteins; or a combination of (i) and (ii); and (e) comparing the components of the complexes isolated...

... from two or more different cell populations one or more types of gene regulatory element complexes formed between cis site-containing or regulatory sequence-containing *nucleic* acid molecules and associated protein components; (b) detecting and analyzing one or more of the *nucleic* acid molecule or associated protein components comprising the complexes of the cell populations; and (c) comparing the *nucleic* acid molecule or protein components from the cell populations so as to determine global gene regulatory element activity in the two or more cell populations, or a global analysis of transcription events occurring in the two or more cell populations. The cis sites contained in the *nucleic* acid molecules of the complexes of the cell populations are identified by isolating the *nucleic* acid molecules or fragments, and determining cis site-containing *nucleic* acid sequences. Cis sites contained in the *nucleic* acid molecules of the complexes of the cell populations are identified by amplifying fragments obtained from the *nucleic* acid molecules of the complexes and obtaining overlapping or nonoverlapping fragments, where the obtained fragments are further size-selected and concatamerized for cloning and sequencing. The fragments are 50-100 base pairs in length. The *nucleic* acid molecules or fragments, of the complexes of the cell populations are hybridized to probes having known *nucleic* acid sequences under conditions suitable for hybrid formation, where the sequence of a *nucleic* acid molecule or fragment is determined following the formation of hybrids. Prior to hybridization, the *nucleic* acid molecules or fragments are amplified. The method further

comprises a detectable label to allow detection of hybridization complexes. The detectable label comprises a radioactive...

... activity of cells comprises: (a) obtaining from the cells, or from cellular contents obtained from the cells, gene regulatory element complexes comprising cis site-containing *nucleic* acid molecules and associated protein components selected from (i) *nucleic* acid molecules and *nucleic* acid binding proteins; (ii) *nucleic* acid binding proteins and regulatory proteins; (iii) *nucleic* acid molecules, *nucleic* acid binding proteins and regulatory proteins; (iv) *nucleic* acid molecules, *nucleic* acid binding proteins, regulatory proteins and co-regulatory proteins; or (v) combinations, under conditions conducive to the formation of the complexes; (b) detecting the complexes; (c) identifying (i) a *nucleic* acid sequence of one or more cis site-containing *nucleic* acid molecules comprising the complexes, (ii) an amino acid sequence of one or more *nucleic* acid binding proteins, regulatory proteins, or co-regulatory proteins comprising the complexes, or a combination of (i) and (ii), where identification of the *nucleic* acid components of the separated complexes comprises one or more of (1) sequencing the *nucleic* acid molecules or a portion, (2) hybridizing the *nucleic* acid molecules to other known *nucleic* acid molecules, (3) preparing a *recombinant* library from the isolated *nucleic* acid molecules or portions, (4) sequencing the library or a portion, or (5) amplifying the *nucleic* acid sequences to determine if specific *nucleic* acid sequences are present in the isolated *nucleic* acid molecules so as to globally profile gene regulatory element activity in the cells. The complexes of (b) and the sequences of (c) are compared...

... comprises fluorescent polarization, direct detection comprising a fluorescent label or a chemiluminescent label, or separating the complexes from exogenous material. The complexes are separated from *nucleic* acid molecules and proteins not comprising the complexes before the detecting step. Separation is performed by electrophoretic mobility shift assay (EMSA), capillary electrophoresis (CE), filtration, size-exclusion filtration, affinity purification, enzyme digestion, or centrifugation. The cis site-containing *nucleic* acid molecules are contacted with a surface comprising a macroarray or a microarray. Alternatively, determining a global gene regulatory element activity profile of cells comprises...

... least one cell, or from cellular contents obtained from at least one cell, one or more types of gene regulatory element complexes formed between cellular *nucleic* acid and associated protein components, the complexes comprising: (i) *nucleic* acid molecules and *nucleic* acid binding proteins, (ii) *nucleic* acid binding proteins and regulatory proteins, (iii) *nucleic* acid molecules, *nucleic* acid binding proteins and regulatory proteins, (iv) *nucleic* acid molecules, *nucleic* acid binding proteins, regulatory proteins and co-regulatory proteins, or (v) combinations, under conditions conducive to the formation of the complexes; (b) separating the one or more types of complexes from other complexes and/or from unbound components; (c) identifying (i) the *nucleic* acid components of the separated complexes, or (ii) the protein components of the separated complexes; and(d) combining activity information of at least two of the complexes to generate a global gene regulatory element activity profile for the cells. The *nucleic* acid molecules of the complexes are fragmented before separating the complexes. They are fragmented using sonication, restriction enzyme digestion, nuclease digestion, pH or elevation of...

... Separating at least one type or class of complexes comprises use of affinity reagents. The affinity reagents include antibodies that recognize transcription-associated proteins or *nucleic* acid probes that recognize transcription-associated *nucleic* acids. Separating comprises physical separation of the complexes based on molecular size, charge, molecular weight, or recognition of molecular moieties. Identifying comprises quantification of the number of *nucleic* acid sequences comprising the complexes. Identifying the *nucleic* acid components of the separated complexes comprises sequencing the *nucleic* acid molecules or a portion; hybridizing the *nucleic* acid molecules to other known *nucleic* acid molecules, amplifying the *nucleic* acids, or generating a *recombinant* library from the isolated *nucleic* acid molecules, or portions; and (i) sequencing the library or a portion, or (ii) amplifying the *nucleic* acids, to determine if specific *nucleic* acid sequences are present in the isolated *nucleic* acid molecules. Generating a *recombinant* library comprises ligating random primers to the ends of the isolated *nucleic* acid molecules or portions; amplifying *nucleic* acid sequences corresponding to the isolated *nucleic* acid molecules or portions; size-fractionating the amplified sequences to a desired size; concatamerizing the amplified molecules into chains of about 5-30 molecules; cloning...

... concatamerized molecules into a suitable cloning vector, growing the clones to obtain more copies, and sequencing inserts of the clones. Identifying also comprises amplifying isolated *nucleic* acids using primers specific for specific sequences in a genome. Amplifying involves PCR, quantitative PCR, ligation-mediated PCR, rolling circle amplification, transcription-mediated amplification, and...

... is performed by (i) binding the proteins from the complexes onto an array comprising antibodies directed toward the protein in the complex, or (ii) binding *nucleic* acid from the complexes onto an array comprising *nucleic* acid molecules of known sequence. The components of the complexes are stably associated before the isolating step. The cells are also subjected to a cross-linking agent prior to the isolating step. *Stable* association of the components results from one or more of chemical cross-linking, biological cross-linking, ultraviolet light cross-linking, or cleavable linker interactions. USE ...

3/3,K/17 (Item 4 from file: 357)

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New immunogenic analogue of a human TNFalpha protein comprising two or three complete TNFalpha monomers, useful in preparing a vaccine composition against a multimeric protein for treating e.g., cancer - liposome or virus vector-mediated gene transfer and expression in bacterium for *recombinant* protein production for use in disease *recombinant* vaccine

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PATENT ASSIGNEE: PHARMEXA AS 2004

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